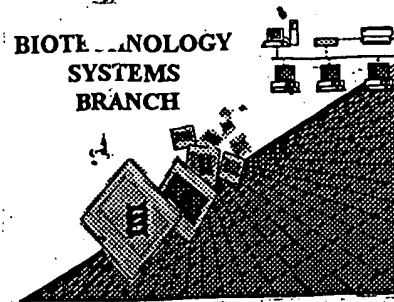


RAW SEQUENCE LISTING **ERROR REPORT**

BIOTECHNOLOGY
SYSTEMS
BRANCH



CS-0010280
0400

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/996,292

Source: OIPE

Date Processed by STIC: 12/6/01

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.

PATENTIN 2.1 e-mail help: patin21help@uspto.gov or phone 703-306-4119 (R. Wax)

PATENTIN 3.0 e-mail help: patin3help@uspto.gov or phone 703-306-4119 (R. Wax)

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 3.0 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW:

Checker Version 3.0

The Checker Version 3.0 application is a state-of-the-art Windows based software program employing a logical and intuitive user-interface to check whether a sequence listing is in compliance with format and content rules. Checker Version 3.0 works for sequence listings generated for the original version of 37 CFR §§1.821 - 1.825 effective October 1, 1990 (old rules) and the revised version (new rules) effective July 1, 1998 as well as World Intellectual Property Organization (WIPO) Standard ST.25.

Checker Version 3.0 replaces the previous DOS-based version of Checker, and is Y2K-compliant. Checker allows public users to check sequence listings in Computer Readable form (CRF) before submitting them to the United States Patent and Trademark Office (USPTO). Use of Checker prior to filing the sequence listing is expected to result in fewer errored sequence listings, thus saving time and money.

Checker Version 3.0 can be down loaded from the USPTO website at the following address:

<http://www.uspto.gov/web/offices/pac/checker>

BEST AVAILABLE COPY

Raw Sequence Listing Error Summary

ERROR DETECTED

SUGGESTED CORRECTION

SERIAL NUMBER: 09/996, 292

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

- 1 Wrapped Nucleics
 Wrapped Aminos The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."

- 2 Invalid Line Length The rules require that a line not exceed 72 characters in length. This includes white spaces.

- 3 Misaligned Amino
 Numbering The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.

- 4 Non-ASCII The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.

- 5 Variable Length Sequence(s) contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.

- 6 PatentIn 2.0
 "bug" A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) . Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.

- 7 Skipped Sequences
 (OLD RULES) Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence:
 (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
 (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
 This sequence is intentionally skipped

 Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.

- 8 Skipped Sequences
 (NEW RULES) Sequence(s) missing. If intentional, please insert the following lines for each skipped sequence.
 <210> sequence id number
 <400> sequence id number
 000

- 9 Use of n's or Xaa's
 (NEW RULES) Use of n's and/or Xaa's have been detected in the Sequence Listing.
 Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
 In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.

- 10 Invalid <213>
 Response Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence

- 11 ✓ Use of <220> Sequence(s) most missing the <220> "Feature" and associated numeric identifiers and responses.
 Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.
 (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)

- 12 PatentIn 2.0
 "bug" Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

OIIPE

RAW SEQUENCE LISTING
PATENT APPLICATION: US/09/996,292

DATE: 12/06/2001
TIME: 11:33:45

Input Set : A:\ISIS4804.ST25.txt
Output Set: N:\CRF3\12062001\I996292.raw

**Does Not Comply
Corrected Diskette Needed**

3 <110> APPLICANT: Manoharan, Muthiah
5 <120> TITLE OF INVENTION: Nuclease Resistant Chimeric Oligonucleotides
7 <130> FILE REFERENCE: ISIS-4804
C--> 9 <140> CURRENT APPLICATION NUMBER: US/09/996,292
C--> 9 <141> CURRENT FILING DATE: 2001-11-28
9 <160> NUMBER OF SEQ ID NOS: 55
11 <170> SOFTWARE: PatentIn version 3.1
13 <210> SEQ ID NO: 1
14 <211> LENGTH: 20
15 <212> TYPE: DNA
16 <213> ORGANISM: Artificial Sequence
18 <220> FEATURE:
19 <223> OTHER INFORMATION: Novel Sequence
21 <220> FEATURE:
22 <221> NAME/KEY: misc_feature
23 <222> LOCATION: (1)..(20)
24 <223> OTHER INFORMATION: All P=S
27 <220> FEATURE:
28 <221> NAME/KEY: misc_feature
29 <222> LOCATION: (1)..(1)
30 <223> OTHER INFORMATION: N= L-Thymidine
33 <220> FEATURE:
34 <221> NAME/KEY: misc_feature
35 <222> LOCATION: (20)..(20)
36 <223> OTHER INFORMATION: N= L-Thymidine
39 <400> SEQUENCE: 1

→ The type of errors shown exist throughout the Sequence Listing. Please check subsequent sequences for similar errors.

- invalid response, see error summary sheet, item 11
(must explain source of genetic material)

W--> 40 ngcatccccc aggccaccan

20

43 <210> SEQ ID NO: 2
44 <211> LENGTH: 17
45 <212> TYPE: DNA
46 <213> ORGANISM: Artificial Sequence
48 <220> FEATURE:
49 <223> OTHER INFORMATION: Novel Sequence
51 <220> FEATURE:
52 <221> NAME/KEY: misc_feature
53 <222> LOCATION: (1)..(17)
54 <223> OTHER INFORMATION: All P=S
57 <220> FEATURE:
58 <221> NAME/KEY: misc_feature
59 <222> LOCATION: (1)..(1)
60 <223> OTHER INFORMATION: N= L-Thymidine
63 <220> FEATURE:
64 <221> NAME/KEY: misc_feature
65 <222> LOCATION: (2)..(3)
66 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
69 <220> FEATURE:
70 <221> NAME/KEY: misc_feature

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/996,292

DATE: 12/06/2001

TIME: 11:33:45

Input Set : A:\ISIS4804.ST25.txt

Output Set: N:\CRF3\12062001\I996292.raw

```

71 <222> LOCATION: (15)..(15)
72 <223> OTHER INFORMATION: N= 2'-O-MOE A
75 <220> FEATURE:
76 <221> NAME/KEY: misc_feature
77 <222> LOCATION: (16)..(16)
78 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
81 <220> FEATURE:
82 <221> NAME/KEY: misc_feature
83 <222> LOCATION: (17)..(17)
84 <223> OTHER INFORMATION: N= L-Thymidine
87 <400> SEQUENCE: 2
W--> 88 nnnccgtgtg atgcnnn 17
91 <210> SEQ ID NO: 3
92 <211> LENGTH: 20
93 <212> TYPE: DNA
94 <213> ORGANISM: Artificial Sequence
96 <220> FEATURE:
97 <223> OTHER INFORMATION: Novel Sequence
99 <220> FEATURE:
100 <221> NAME/KEY: misc_feature
101 <222> LOCATION: (1)..(20)
102 <223> OTHER INFORMATION: All P=S
105 <220> FEATURE:
106 <221> NAME/KEY: misc_feature
107 <222> LOCATION: (1)..(1)
108 <223> OTHER INFORMATION: N= L-Thymidine
111 <220> FEATURE:
112 <221> NAME/KEY: misc_feature
113 <222> LOCATION: (2)..(3)
114 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
117 <220> FEATURE:
118 <221> NAME/KEY: misc_feature
119 <222> LOCATION: (13)..(14)
120 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
123 <220> FEATURE:
124 <221> NAME/KEY: misc_feature
125 <222> LOCATION: (15)..(15)
126 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
129 <220> FEATURE:
130 <221> NAME/KEY: misc_feature
131 <222> LOCATION: (16)..(16)
132 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
135 <220> FEATURE:
136 <221> NAME/KEY: misc_feature
137 <222> LOCATION: (17)..(17)
138 <223> OTHER INFORMATION: N= 2'-O-MOE A
141 <220> FEATURE:
142 <221> NAME/KEY: misc_feature
143 <222> LOCATION: (18)..(19)

```

RAW SEQUENCE LISTING
PATENT APPLICATION: US/09/996,292

DATE: 12/06/2001
TIME: 11:33:45

Input Set : A:\ISIS4804.ST25.txt
Output Set: N:\CRF3\12062001\I996292.raw

```

144 <223> OTHER INFORMATION: N= 2'-O-MOE G
147 <220> FEATURE:
148 <221> NAME/KEY: misc_feature
149 <222> LOCATION: (20)..(20)
150 <223> OTHER INFORMATION: N= L-Thymidine
153 <400> SEQUENCE: 3
W--> 154 nnngtcacgcg ctnnnnnnnnnn 20
157 <210> SEQ ID NO: 4
158 <211> LENGTH: 20
159 <212> TYPE: DNA
160 <213> ORGANISM: Artificial Sequence
162 <220> FEATURE:
163 <223> OTHER INFORMATION: Novel Sequence
165 <220> FEATURE:
166 <221> NAME/KEY: misc_feature
167 <222> LOCATION: (1)..(20)
168 <223> OTHER INFORMATION: All P=S
171 <400> SEQUENCE: 4
172 tgcacccccc aggccacccat 20
175 <210> SEQ ID NO: 5
176 <211> LENGTH: 20
177 <212> TYPE: DNA
178 <213> ORGANISM: Artificial Sequence
180 <220> FEATURE:
181 <223> OTHER INFORMATION: Novel Sequence
183 <220> FEATURE:
184 <221> NAME/KEY: misc_feature
185 <222> LOCATION: (1)..(20)
186 <223> OTHER INFORMATION: All P=S
189 <220> FEATURE:
190 <221> NAME/KEY: misc_feature
191 <222> LOCATION: (1)..(1)
192 <223> OTHER INFORMATION: N= L-Thymidine
195 <220> FEATURE:
196 <221> NAME/KEY: misc_feature
197 <222> LOCATION: (20)..(20)
198 <223> OTHER INFORMATION: N= L-Thymidine
201 <400> SEQUENCE: 5
W--> 202 ngcatccccc aggccaccan 20
205 <210> SEQ ID NO: 6
206 <211> LENGTH: 17
207 <212> TYPE: DNA
208 <213> ORGANISM: Artificial Sequence
210 <220> FEATURE:
211 <223> OTHER INFORMATION: Novel Sequence
213 <220> FEATURE:
214 <221> NAME/KEY: misc_feature
215 <222> LOCATION: (1)..(17)
216 <223> OTHER INFORMATION: All P=S

```

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/996,292

DATE: 12/06/2001

TIME: 11:33:45

Input Set : A:\ISIS4804.ST25.txt

Output Set: N:\CRF3\12062001\I996292.raw

```

219 <400> SEQUENCE: 6
220 tcccgtgtg atgcatt
223 <210> SEQ ID NO: 7
224 <211> LENGTH: 17
225 <212> TYPE: DNA
226 <213> ORGANISM: Artificial Sequence
228 <220> FEATURE:
229 <223> OTHER INFORMATION: Novel Sequence
231 <220> FEATURE:
232 <221> NAME/KEY: misc_feature
233 <222> LOCATION: (1)..(17)
234 <223> OTHER INFORMATION: All P=S
237 <220> FEATURE:
238 <221> NAME/KEY: misc_feature
239 <222> LOCATION: (1)..(1)
240 <223> OTHER INFORMATION: N= L-Thymidine
243 <220> FEATURE:
244 <221> NAME/KEY: misc_feature
245 <222> LOCATION: (2)..(3)
246 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
249 <220> FEATURE:
250 <221> NAME/KEY: misc_feature
251 <222> LOCATION: (15)..(15)
252 <223> OTHER INFORMATION: N= 2'-O-MOE A
255 <220> FEATURE:
256 <221> NAME/KEY: misc_feature
257 <222> LOCATION: (16)..(16)
258 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
261 <220> FEATURE:
262 <221> NAME/KEY: misc_feature
263 <222> LOCATION: (17)..(17)
264 <223> OTHER INFORMATION: N= L-Thymidine
267 <400> SEQUENCE: 7
W--> 268 nnncgctgtg atgcnnn
271 <210> SEQ ID NO: 8
272 <211> LENGTH: 20
273 <212> TYPE: DNA
274 <213> ORGANISM: Artificial Sequence
276 <220> FEATURE:
277 <223> OTHER INFORMATION: Novel Sequence
279 <220> FEATURE:
280 <221> NAME/KEY: misc_feature
281 <222> LOCATION: (1)..(20)
282 <223> OTHER INFORMATION: All P=S
285 <220> FEATURE:
286 <221> NAME/KEY: misc_feature
287 <222> LOCATION: (1)..(1)
288 <223> OTHER INFORMATION: N= L-Cytidine
291 <220> FEATURE:

```

RAW SEQUENCE LISTING

DATE: 12/06/2001

PATENT APPLICATION: US/09/996,292

TIME: 11:33:45

Input Set : A:\ISIS4804.ST25.txt

Output Set: N:\CRF3\12062001\I996292.raw

292 <221> NAME/KEY: misc_feature
 293 <222> LOCATION: (2)..(2)
 294 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
 297 <220> FEATURE:
 298 <221> NAME/KEY: misc_feature
 299 <222> LOCATION: (3)..(3)
 300 <223> OTHER INFORMATION: N= 2'-O-MOE A
 303 <220> FEATURE:
 304 <221> NAME/KEY: misc_feature
 305 <222> LOCATION: (4)..(4)
 306 <223> OTHER INFORMATION: N= 2'-O-MOE G
 309 <220> FEATURE:
 310 <221> NAME/KEY: misc_feature
 311 <222> LOCATION: (5)..(5)
 312 <223> OTHER INFORMATION: N= 2'-O-MOE A
 315 <220> FEATURE:
 316 <221> NAME/KEY: misc_feature
 317 <222> LOCATION: (16)..(16)
 318 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
 321 <220> FEATURE:
 322 <221> NAME/KEY: misc_feature
 323 <222> LOCATION: (17)..(17)
 324 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
 327 <220> FEATURE:
 328 <221> NAME/KEY: misc_feature
 329 <222> LOCATION: (18)..(18)
 330 <223> OTHER INFORMATION: N= 2'-O-MOE G
 333 <220> FEATURE:
 334 <221> NAME/KEY: misc_feature
 335 <222> LOCATION: (19)..(19)
 336 <223> OTHER INFORMATION: N= 2'-O-MOE 5meU
 339 <220> FEATURE:
 340 <221> NAME/KEY: misc_feature
 341 <222> LOCATION: (20)..(20)
 342 <223> OTHER INFORMATION: N= 2'-O-MOE 5meC
 345 <400> SEQUENCE: 8

W--> 346 nnnnnttcca cactcnnnnn

20

349 <210> SEQ ID NO: 9
 350 <211> LENGTH: 20
 351 <212> TYPE: DNA
 352 <213> ORGANISM: Artificial Sequence
 354 <220> FEATURE:
 355 <223> OTHER INFORMATION: Novel Sequence
 357 <220> FEATURE:
 358 <221> NAME/KEY: misc_feature
 359 <222> LOCATION: (1)..(20)
 360 <223> OTHER INFORMATION: All P=S
 363 <220> FEATURE:
 364 <221> NAME/KEY: misc_feature

VERIFICATION SUMMARY

DATE: 12/06/2001

PATENT APPLICATION: US/09/996,292

TIME: 11:33:46

Input Set : A:\ISIS4804.ST25.txt

Output Set: N:\CRF3\12062001\I996292.raw

L:9 M:270 C: Current Application Number differs, Replaced Current Application No

L:9 M:271 C: Current Filing Date differs, Replaced Current Filing Date

L:40 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1

L:88 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2

L:154 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3

L:202 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:5

L:268 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:7

L:346 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:8

L:424 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:9

L:502 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10

L:568 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:11

L:640 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:12

L:688 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:13

L:736 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:14

L:790 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:15

L:868 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:16

L:934 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:17

L:1012 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:18

L:1078 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:19

L:1156 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:20

L:1234 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:21

L:1312 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:22

L:1396 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:23

L:1462 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:24

L:1534 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:25

L:1613 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:26

L:1693 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:27

L:1772 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:28

L:1852 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:29

L:1930 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:30

L:2008 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:31

L:2086 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:32

L:2166 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:33

L:2184 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:34

L:2202 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:35

L:2220 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:36

L:2238 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:37

L:2262 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:38

L:2286 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:39

L:2322 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:41

L:2364 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:43

L:2388 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:44

L:2412 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:45

L:2436 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:46

L:2460 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:47

L:2484 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:48

L:2508 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:49

L:2538 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:51

VERIFICATION SUMMARY

PATENT APPLICATION: US/09/996,292

DATE: 12/06/2001

TIME: 11:33:46

Input Set : A:\ISIS4804.ST25.txt

Output Set: N:\CRF3\12062001\I996292.raw

L:2556 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:52
L:2580 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:53
L:2598 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:54
L:2616 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:55